

WHAT IS CLAIMED IS:

Sub 1
1. A method for delivery of a pharmaceutical composition to gastrointestinal cells in a recipient in need thereof which comprises:

- 2
3 (a) contacting the intended site of delivery of said pharmaceutical composition with an
4 agent adequate to cause a temporary disruption of the mucosal lining covering said
5 gastrointestinal cells; and
6 (b) concurrently or subsequent to said contacting of step (a), contacting said
7 gastrointestinal or genitourinary cells with said pharmaceutical composition, wherein
8 said pharmaceutical composition comprises a nucleic acid or a cell comprising a
9 nucleic acid, the expression of which is desired in said gastrointestinal cells.

1 2. The method according to claim 1 wherein said pharmaceutical composition further comprises
2 a protein, an antibiotic, an anti-inflammatory, an analgesic, an anti-neoplastic, a cell, or a
3 mixture thereof.

1 3. The method according to claim 2 wherein said pharmaceutical composition comprises a
2 nucleic acid or a cell comprising a nucleic acid encoding (i) an RNA product which is the
3 antisense of a gene product, the expression of which is intended to be suppressed in said
4 gastrointestinal cells or (ii) a peptide or protein the expression of which is desired in said
5 gastrointestinal cells.

1 4. The method according to claim 3 wherein said protein is a biologically active protein capable
2 of effecting desired biological functions or is an immunogenic protein against which immune
3 responses are intended to be induced.

1 5. The method according to claim 4 wherein said protein is selected from the group consisting
2 of a tumor antigen, a cytokine, a growth factor, a marker gene product, an enzyme, a
3 receptor, a receptor antagonist, and a structural protein.

1 6. The method according to claim 5 wherein said tumor antigen is the PymT antigen, wherein
2 said growth factor or cytokine is an interleukin or is a tissue growth factor, and wherein said
3 receptor antagonist is an interleukin receptor or growth factor antagonist.

1 7. The method according to claim 3 wherein said nucleic acid comprises sufficient gene
2 regulatory control sequences to achieve efficient expression of encoded sequences upon
3 uptake of said nucleic acid by said gastrointestinal or genitourinary cells.

1 8. The method according to claim 4 wherein said nucleic acid comprises viral sequences.

1 9. The method according to claim 8 wherein said viral sequences are selected from adenoviral
2 sequences and retroviral sequences.

1 10. The method according to claim 9 wherein said adenoviral sequences are insufficient to
2 encode a replication-competent virus in the absence of adenoviral sequences or functions
3 provided in trans.

1 11. The method according to claim 1 wherein said agent adequate to cause a temporary
2 disruption of the mucosal lining covering said gastrointestinal or genitourinary cells is a
3 mucolytic agent, a mucodisruptive agent, a penetration enhancing agent, or a combination
4 of such agents.

1 12. The method according to claim 11 wherein said agent is administered by means of a spray,
2 suppository, or enema.

1 13. The method according to claim 12 wherein said agent is selected from the group consisting
2 of a ~~non-toxic~~ alcohol, DMSO, a mucolytic enzyme, N-acetyl cysteine, and combinations
3 thereof.

1 14. The method according to claim 13 wherein said alcohol is ethyl alcohol.

1 15. The method according to claim 14 wherein said ethyl alcohol comprises about a 5 to 75%
2 concentration of ethyl alcohol.

1 16. The method according to claim 15 wherein said ethyl alcohol comprises about a 25 to 60%
2 concentration of ethyl alcohol.

1 17. The method according to claim 15 wherein said ethyl alcohol comprises about a 50%
2 concentration of ethyl alcohol.

1 18. The method according to claim 1 which comprises intrarectal administration of about a 50%
2 solution of ethyl alcohol about three hours prior to administration of a nucleic acid encoding
3 a gene product the expression of which in intestinal epithelial and other intestinal cells is
4 desired.

1 19. The method according to claim 18 wherein said nucleic acid encodes a gene product selected
2 from the group consisting of tumor antigen, a growth factor, a cytokine, a receptor, a receptor
3 antagonist, a structural protein, an antisense nucleic acid, an antigen encoded by a pathogen
4 against which immune responses are desired to be elicited, and combinations thereof.

1 20. A method for inducing extended transgene expression in the intestine which comprises
2 simultaneous treatment or pre-treatment of the intestinal tract with a mucous membrane
3 disruptive agent and contacting the thus treated intestinal tract with a nucleic acid.

1 21. The method of claim 20 wherein said nucleic acid comprises a biologically active gene.

1 22. The method according to claim 21 wherein said nucleic acid is contained within a vector or
2 a cell.

1 23. The method according to claim 20 wherein said nucleic acid is in a precipitated or
2 encapsulated state, such that nucleic acid is released for uptake by intestinal cells over an
3 extended period of time.

1 24. The method according to claim 20 wherein said method is repeated.

1 25. A composition comprising a mucolytic agent or a mucodisruptive agent in combination with
2 a biologically active nucleic acid.

Sub 2
1 26. A suppository comprising a biologically active nucleic acid.

1 27. A method for treating or preventing a pathologic condition which comprises temporary
2 disruption of the mucosal lining of the intestine and contact of the thus treated intestine with
3 a biologically active nucleic acid.

28. The method according to claim 27 for prevention or treatment of intestinal tumors, treatment
or prevention of sexually transmitted diseases, or treatment or prevention of inflammatory
bowel disease.

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